

Atty. Docket No. 047714-5004-US

Application No. 09/068,935

Page 2

55. A vaccine comprising a pharmaceutically acceptable carrier and an isolated pathogen adhesin molecule or immunogenic fragment thereof, wherein the pathogen adhesin molecule or immunogenic fragment thereof specifically binds to an adhesion molecule on a host cell or extracellular matrix under shear conditions *in vitro*, and wherein said vaccine induces a therapeutically effective immune response against the pathogen.

56. The vaccine of claim 55, wherein said shear conditions are selected from the group consisting of physiological shear conditions as characteristically found in the: (1) vascular system; (2) respiratory system; (3) gastrointestinal tract; and (4) urinary tract.

C1  
57. The vaccine of claim 55, wherein said host cell is selected from the group consisting of leukocytes, endothelial cells, epithelial cells and cells of the nervous system.

Sub Dkt  
58. The vaccine of claim 55, wherein said pathogen adhesin molecule mimics an adhesion molecule of the host.

59. The vaccine of claim 55, wherein said host adhesion molecule is a receptor for a host ligand selected from the group consisting of C-type lectins, selectins, integrins, members of the immunoglobulin superfamily and cytokines.

60. The vaccine of claim 59, wherein said selectins are selected from the group consisting of E-selectin, L-selectin and P-selectin.

61. The vaccine of claim 59, wherein said integrin is selected from the group consisting of VLA-1, VLA-2, VLA-3, VLA-4, VLA-5, VLA-6, leucam, Mac-1, LFA-1, gp150.95, CD41a, CD49 and CD51.

Atty. Docket No. 047714-5004-US

Application No. 09/068,935

Page 3

Sub  
DHT

62. The vaccine of claim 59, wherein said member of the immunoglobulin superfamily is selected from the group consisting of ICAM-1, ICAM-2 or ICAM-3, VCAM, NCAM and PECAM.

63. The vaccine of claim 55, wherein said host adhesion molecule is selected from the group consisting of proteins, glycoproteins, glycolipids and carbohydrates.

Sub  
DHT

64. The vaccine of claim 55, wherein said pathogen adhesin molecule binds to a carbohydrate ligand selected from the group consisting of residues of N-acetylneuraminic acid, sialic acid, N-acetylglucosamine, N-acetylgalactosamine, glucosamine, galactosamine, galactose, mannose, fucose and lactose.

C1

65. The vaccine of claim 55 wherein said host adhesion molecule is a guanosine triphosphate-binding protein.

66. The vaccine of claim 55, but wherein said guanosine triphosphate-binding protein is selected from the group consisting of Rho, Ras, Rac, Dcd42, Rab, Ran and Arf.

67. The vaccine of claim 55 wherein said host cell is selected from the group consisting of cytokine-stimulated endothelial cells and endothelial cells expressing ICAM-1, CAM-1, MAdCAM-1 and PNAAd-1.

68. The vaccine of claim 55, wherein said pathogen is selected from the group consisting of viruses, bacteria, protozoa and fungi.

69. The vaccine of claim 68, wherein said pathogen is a virus.

Atty. Docket No. 047714-5004-US

Application No. 09/068,935

Page 4

70. The vaccine of claim 68, wherein said pathogen is a bacterium.

71. The vaccine of claim 68, wherein said pathogen is a protozoa.

72. The vaccine of claim 68, wherein said pathogen is a fungus.

C) 73. The vaccine of claim 68, wherein the pathogen is an intestinal tract pathogen selected from the group consisting of *Vibrio cholerae*, uropathogenic *Escherichia coli*, enterohemorrhagic *E. coli*, enteropathogenic *E. coli*, *Salmonella* species, *Shigella* species, *Pseudomonas* species, *Proteus* species, *Klebsiella pneumoniae*, *Aerobacter aerogenes*, and *Helicobacter pylori*.

74. The vaccine of claim 68, wherein said pathogen is selected from the blood cell group consisting of *Plasmodium berghei*, *Plasmodium falciparum*, *Brucella* species, *Neisseria meningitidis*, *Staphylococcus* species, *Pasteurella pestis*, *Leishmania*, *Trypanosoma* and *Pasteurella tularensis*.

75. The vaccine of claim 68, wherein said pathogen is selected from the group consisting of *Mycobacterium tuberculosis*, *Legionella*, *Staphylococcus* species, *Streptococcus* species, *Bordetella pertussis*, *Pasteurella pestis*, *Hemophilus influenzae*, and *Corynebacterium diphtheriae*.

76. The vaccine of claim 68, wherein said pathogen is selected from the fungal parasite group consisting of *Blastomyces*, *Aspergillus*, *Cryptococcus*, *Candida*, *Histoplasma*, *Coccidioides* and *Phycomycetes*.

Atty. Docket No. 047714-5004-US

Application No. 09/068,935

Page 5

77. The vaccine of claim 68, wherein said pathogen is selected from the intestinal parasite group consisting of *Entamoeba histolytica*, *Giardia lamblia*, and *Cryptosporidium*.

78. The vaccine of claim 68, wherein said pathogen is selected from the genito-urinary tract group consisting of *Neisseria gonorrhoeae*, *Chlamydia*, *Treponema pallidum*, *Trichomonas vaginalis*, and *Tritrichomonas foetus*.

U 79. The vaccine of claim 68, wherein said pathogen is selected from the virus group consisting of *Influenza A*, *Influenza B*, *Influenza C*, *Measles virus*, *Mumps virus*, *Adenovirus*, *Rhinovirus*, *Poliovirus*, *Hepatitis virus*, *Hantavirus*, *Herpesvirus*, *Rubella*, *Human Immunodeficiency virus (HIV)* and *Coxsackieviruses*.

80. The vaccine of claim 55, wherein said host cell is selected from the group of respiratory system cells consisting of alveolar macrophages and endothelial and epithelial cells of the nasopharynx and alveoli.

81. The vaccine of claim 55, wherein said vaccine further comprises peptide domains of the adhesive region on the  $\beta$ -oligomer of an exotoxin selected from a group consisting of *Corynebacterium diphtheriae* exotoxin, *Bordetella pertussis* toxin, *Shigella dysenteriae* (Type I) toxin, *Salmonella typhimurium* toxin, *Vibrio cholerae* toxin, enterhemorrhagic *Escherichia coli* verotoxin, Enteropathogenic *Escherichia coli* enterotoxin, *Pseudomonas aeruginosa* exotoxin, *Clostridium tetani* exotoxin and *Clostridium botulinum* exotoxin.

82. The vaccine of claim 55, wherein said vaccine further comprises peptide domains of the adhesive lectin region on fimbriae displayed on microbes selected from a group consisting

Atty. Docket No. 047714-5004-US  
Application No. 09/068,935  
Page 6

of *Escherichia coli*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Salmonella typhi*, *Salmonella typhimurim*, other *Salmonella* species, *Pseudomonas aeruginosa* and *Yersinia enterocolitica*.

83. The vaccine of claim 55, wherein said vaccine further comprises peptide domains of glycoprotein adhesion molecules on the cell surface of microbes selected from a group consisting of *Escherichia coli*, *Yersinia pseudotuberculosis*, *Helicobacter pylori*, *Vibrio cholera*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella dysenteriae*, *Leishmania*, *Giardia lamblia*, *Entamoeba histolytica*, *Candida albicans* and *Harnia alvae*.

cl 84. The vaccine of claim 55, wherein said vaccine further comprises peptide domain of glycoprotein adhesion molecules that bind to sialic acid ligands on nervous systems cells.

85. The vaccine of claim 55, wherein said vaccine comprises peptide domains of a microbial glycoprotein adhesion molecule selected from a group consisting of *Neisseria meningitidis* and *Escherichia coli* K1.

86. The vaccine of claim 55, further comprising a delivery system displaying said pathogen adhesion molecule or immunogenic fragment thereof.

87. The vaccine of claim 86, where said delivery system is selected from the group consisting of phage, a live vector, liposomes, M13 phage, cowpea mosaic virus, alginate gels, peptide conjugates, and glycoconjugates.

88. The vaccine of claim 87, wherein said live vector is a *Salmonella* species, a *Shigella* species or adenovirus.

Atty. Docket No. 047714-5004-US  
Application No. 09/068,935  
Page 7

89. A vaccine comprising a pharmaceutically acceptable carrier and an isolated pathogen adhesin molecule or immunogenic fragment thereof, wherein the pathogen adhesin molecule specifically binds to an adhesion molecule on a host cell or extracellular matrix under physiologic shear conditions *in vitro*, and wherein said vaccine induces a therapeutically effective immune response against the pathogen.

90. A vaccine comprising a pharmaceutically acceptable carrier and an isolated pathogen adhesin molecule mimetic, wherein said mimetic induces a therapeutically effective immune response against the pathogen.

C1 91. A method of obtaining a vaccine against a pathogen comprising the steps of:

- (a) selecting a pathogen adhesin molecule or fragments thereof that specifically binds to an adhesion molecule on a host cell or extracellular matrix;
- (b) developing one or more monoclonal antibodies (mAbs) directed against at least one region of the isolated adhesin molecule or fragments thereof;
- (c) isolating epitopes bound by said mAbs; and
- (d) screening said selected epitopes to identify a molecule that induces a therapeutically effective immune response against the pathogen.

92. The method of claim 91, wherein said step of selecting is performed by a shear assay using target cells that express the host adhesion molecule.

93. The method of claim 91, further comprising a step of analyzing the specificity and blocking properties of mAbs for the pathogen/host cell interactions by a shear assay.

Atty. Docket No. 047714-5004-US  
Application No. 09/068,935  
Page 8

94. The method of claim 91 wherein said step of isolating epitopes includes screening a phage display library to identify mimetics of the pathogen adhesin molecule that also bind to said one or more monoclonal antibodies.

95. A diagnostic assay kit, comprising a monoclonal antibody specific for a pathogen adhesin molecule, wherein said molecule is capable of binding specifically to an adhesion molecule on a host cell or extracellular matrix under shear conditions *in vitro*.

96. The diagnostic assay kit of claim 95, wherein said pathogen adhesin molecule mimics an adhesion molecule of the host.

97. The diagnostic assay kit of claim 95, further comprising superparamagnetic beads coated with said monoclonal antibodies.

98. A diagnostic assay kit, comprising a peptide or oligopeptide that mimics the adhesive domain of a pathogen adhesin molecule, wherein said molecule [is capable of binding] specifically binds to an adhesion molecule on a host cell or extracellular matrix under shear conditions *in vitro*.

99. A diagnostic assay test composition comprising a glycolipid matrix displaying host adhesion molecules presenting a residue selected from the group consisting of residues of N-acetylneuraminic acid, sialic acid, N-acetylglucosamine, N-acetylgalactosamine, glucosamine, galactosamine, galactose, mannose, fucose and lactose; wherein said host adhesion molecule binds specifically to a pathogen adhesin molecule under shear conditions *in vitro*.

Atty. Docket No. 047714-5004-US

Application No. 09/068,935

Page 9

100. A therapeutic composition comprising a pharmaceutically acceptable carrier and an isolated pathogen adhesin molecule or fragment thereof, wherein said pathogen adhesin molecule or fragment [is capable of binding] specifically binds to an adhesion molecule on a host cell or extracellular matrix under shear conditions *in vitro*.

cl 101. The therapeutic composition of claim 100, wherein said composition inhibits one or more of the following events associated with infection by the pathogen of an infected host, said events being selected from the group consisting of: (1) recognition by the pathogen of specific host cells or extracellular matrix; (2) shear dependent attachment of the pathogen to host cells or extracellular matrix; (3) activation dependent adhesion of the pathogen; (4) signal transduction mediated by the pathogen; (5) transendothelial migration of the pathogen; (6) passage by the pathogen through epithelia; (7) colonization by the pathogen; and (8) binding of a toxin produced by the pathogen to host cells or extracellular matrix.

102. The therapeutic composition of claim 100, wherein said composition binds to members of the selectin family of host adhesion molecules.

103. The therapeutic composition of claim 100, wherein said composition binds to members of the immunoglobulin superfamily of host adhesion molecules.

104. The therapeutic composition of claim 100, wherein said composition binds to members of the integrin family of host adhesion molecules.

Sub  
DIA 105. The therapeutic composition of claim 100, wherein said pathogen adhesin molecule mimics an adhesion molecule of the host.



Atty. Docket No. 047714-5004-US

Application No. 09/068,935

Page 10

106. The therapeutic composition of claim 105, wherein the host adhesion molecule is a receptor for a host ligand selected from the group consisting of selectins, integrins, members of the immunoglobulin superfamily, cytokines and guanosine triphosphate-binding proteins.

107. The therapeutic composition of claim 106, wherein said selectin is selected from the group consisting of E-selectin, L-selectin and P-selectin.

108. The therapeutic composition of claim 106, wherein said integrin is selected from the group consisting of VLA-1, VLA-2, VLA-3, VLA-4, VLA-5, VLA-6, leucam, Mac-1, LFA-1, gp150.95, CD41a, CD49 and CD51.

CI  
Sub DSO  
109. The therapeutic composition of claim 106, wherein said member of the immunoglobulin superfamily is selected from the group consisting of ICAM-1, ICAM-2 or ICAM-3, VCAM, NCAM and PECAM.

110. The therapeutic composition of claim 106, wherein said host adhesion molecule is a guanosine triphosphate-binding protein.

111. The therapeutic composition of claim 110, wherein said guanosine triphosphate-binding protein is selected from the group consisting of Rho, Ras, Rac, Dcd42, Rab, Ran and Arf.

---